

6. (Currently amended) ~~A binding moiety~~ The modified VLD according to claim 3, wherein in which the size of the CDR loop structure is increased by at least nine amino acid residues.

7. (Currently amended) ~~A binding moiety~~ The modified VLD according to claim 1 or claim 3, wherein in which the binding affinity of the modified VLD is altered when compared with the unmodified VLD.

8. (Currently amended) ~~A binding moiety~~ The modified VLD according to claim 7, wherein in which the affinity of the modified VLD to at least one natural ligand of the unmodified VLD is reduced.

9. (Currently amended) ~~A binding moiety~~ The modified VLD according to claim 1 or claim 3, wherein in which the binding specificity of the modified VLD is different [[to]] than that of the unmodified VLD.

10. (Currently amended) ~~A binding moiety~~ The modified VLD according to claim 1 or claim 3, wherein in which the non-antibody ligand is a T-cell surface protein.

11. (Currently amended) ~~A binding moiety~~ The modified VLD according to claim 10, wherein in which the non-antibody ligand is CTLA-4, CD28 or ICOS.

12. (Currently amended) ~~A binding moiety~~ The modified VLD according to claim 11, wherein in which the non-antibody ligand is CTLA-4.

13. (Currently amended) ~~A binding moiety~~ The modified VLD according to claim 1 or claim 3, wherein in which one or more of the CDR loop structures is replaced with a binding determinant derived from a non-antibody polypeptide.

14. (Currently amended) ~~A binding moiety~~ The modified VLD according to claim 13, wherein in which the binding determinant is derived from somatostatin or haemagglutinin.

15. (Currently amended) ~~A binding moiety~~ The modified VLD according to claim 1 or claim 3, wherein in which one or more of the CDR loop structures is replaced with one or more CDR loop structures derived from an antibody or antibodies.

16. (Currently amended) ~~A binding moiety~~ The modified VLD according to claim 15, wherein in which the antibody or antibodies are derived from a rat, mouse, human, camel, llama or shark.

17. (Currently amended) ~~A binding moiety~~ The modified VLD according to claim 15, wherein in which the antibody or antibodies are selected from the camel antibody cAB-Lys3 and the human anti-melanoma antibody V86.

18. (Currently amended) ~~A binding moiety~~ The modified VLD according to claim 1 or claim 3 linked to a diagnostic reagent.

19. (Currently amended) ~~A binding moiety~~ The modified VLD according to claim 18, wherein in which the diagnostic reagent is selected from the group consisting of streptavidin, biotin, a radioisotope, a dye marker or other and an imaging reagent.

20. (Currently amended) A multivalent reagent comprising two or more ~~binding moieties~~ modified VLDs as claimed in claim 1.

21. (Currently amended) ~~A binding moiety~~ The modified VLD or multivalent reagent according to any one of claims 1, 3 or 20, immobilised on a solid support or coupled to a biosensor surface.

22. (Currently amended) A polynucleotide encoding ~~a binding moiety~~ the modified VLD or multivalent reagent as claimed in any one of claims 1, 3 or 20.

23. (Currently amended)) A vector comprising ~~[[a]]~~ the polynucleotide according to claim 22.

24. (Currently amended) A host cell transformed with ~~[[a]]~~ the vector as claimed in claim 22.

25. (Currently amended) ~~[[A]]~~ The host cell according to claim 24, wherein in which the cell is a bacterial cell.

26. (Currently amended) A method of producing ~~a binding moiety~~ a modified monomeric non-antibody ligand VLD which comprises culturing ~~[[a]]~~ the host cell as claimed in claim 24 under conditions enabling expression of the ~~binding moiety~~ modified VLD and optionally recovering the ~~binding moiety~~ modified VLD.

27. (Currently amended) A method according to claim 26, wherein in which the ~~binding moiety~~ modified VLD is unglycosylated.

28. (Currently amended) A composition in a pharmaceutically acceptable carrier or diluent comprising a modified VLD or multivalent reagent as claimed in any one of claims 1, 3 or 20.

29. (Currently amended) A method of treating a pathological condition in a subject, which method comprises administering to the subject a modified V-like domain or multivalent reagent binding moiety as claimed in ~~claim~~ any one of claims 1, 3 or 20.

30. (Currently amended) A method of selecting a binding moiety with an affinity for a target molecule, the method comprising which comprises screening a library of polynucleotides for expression of a binding moiety with an affinity for the target molecule, wherein each polynucleotide encodes a modified monomeric non-antibody ligand VLD, the polynucleotides encoding VLDs derived from one or more non-antibody ligands, wherein the polynucleotides have been subjected to mutagenesis which results in a modification or replacement in at least one CDR loop structure in at least one VLD and wherein the solubility of the isolated modified VLD is improved when compared with ~~the~~ an isolated unmodified VLD.

31. (Currently amended) [[A]] The method according to claim 30, wherein in which the screening process involves displaying the modified V-like domains as gene III protein fusions on the surface of bacteriophage particles.

32. (Currently amended) [[A]] The method according to claim 30, wherein in which the screening process involves displaying the modified V-like domains in a ribosomal display selection system.

33. (Cancelled)

34. (New) The modified VLD according to claim 1 or claim 3, wherein at least two CDR loop structures or parts thereof are modified or replaced.

35. (New) The modified VLD according to claim 1 or claim 3, wherein three CDR loop structures or parts thereof are modified or replaced.

36. (New) At least one modified monomeric non-antibody ligand V-like domain (VLD) comprising at least one CDR loop structure or part thereof that is modified or replaced, such that the solubility of the modified VLD is improved, when compared with an unmodified VLD, wherein the monomeric VLD is a binding moiety, and wherein the non-antibody ligand is a T-cell surface protein.

37. (New) A modified monomeric non-antibody ligand V-like domain (VLD) comprising at least one CDR loop structure or part thereof that is modified or replaced, such that

- (i) the size of the CDR loop structure is altered when compared with the corresponding CDR loop structure in an unmodified VLD; and/or

- (ii) the modification or replacement results in formation of a disulphide bond within or between one or more of the CDR loop structures,

wherein the non-antibody ligand is a T-cell surface protein.

38. (New) At least one modified monomeric non-antibody ligand V-like domain (VLD) comprising at least one CDR loop structure or part thereof that is modified or replaced, such that the solubility of the modified VLD is improved, when compared with an unmodified VLD, wherein the monomeric VLD is a binding moiety, and wherein the non-antibody ligand is CTLA-4, CD28 or ICOS.

39. (New) A modified monomeric non-antibody ligand V-like domain (VLD) comprising at least one CDR loop structure or part thereof that is modified or replaced, such that

- (i) the size of the CDR loop structure is altered when compared with the corresponding CDR loop structure in an unmodified VLD; and/or
- (ii) the modification or replacement results in formation of a disulphide bond within or between one or more of the CDR loop structures,

wherein the non-antibody ligand is CTLA-4, CD28 or ICOS.

40. (New) A modified monomeric non-antibody ligand V-like domain (VLD) comprising at least one CDR loop structure or part thereof that is modified or replaced, such that the solubility of the modified VLD is improved, when compared with an unmodified VLD, wherein the monomeric VLD is a binding moiety.

41. (New) The modified VLD according to claim 3, wherein the size of the CDR loop structure is increased by one amino acid residue.

In the Abstract of the Disclosure

Please replace the Abstract of the Disclosure with the following:

--The present invention relates to ~~new~~ binding moieties comprising at least one monomeric V-like domain (VLD) derived from a non-antibody ligand, the at least one monomeric V-like domain being characterized in that at least one CDR loop structure or part thereof is modified or replaced such that the solubility of the modified VLD is improved when compared with the unmodified VLD.--